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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,464	05/03/2007	Marsha A. Moses	C1285.70006US01	5882
23628	7590	03/15/2011	EXAMINER	
WOLF GREENFIELD & SACKS, P.C.			HARRIS, ALANA M	
600 ATLANTIC AVENUE			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/585,464	MOSES ET AL.
	Examiner Alana M. Harris, Ph.D.	Art Unit 1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 23 February 2011.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,3,4,6,7,9-16 and 20-37 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,3,4,6,7,9-16 and 20-37 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) Notice of Informal Patent Application
- 6) Other: _____

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 23, 2011 has been entered.
2. Claims 1, 3, 4, 6, 7, 9-16 and 20-37 are pending.
Claims 38-55 have been cancelled.
Claims 1, 3, 4, 6, 7, 9-16 and 20-37 are examined on the merits.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Grounds of Rejection

Claim Rejections - 35 USC § 102

4. The rejection of claims 44-46, 48-50, 52-54 under 35 U.S.C. 102(b) as being anticipated by WO document, WO 01/66557 A1 (published 13 September

2001/ IDS reference number 3 submitted May 25, 2010) is withdrawn in light of the cancellation of the claims.

5. The rejection of claims 38-49, 51-53 and 55 under 35 U.S.C. 102(e) as being anticipated by Berger et al./ U.S. Patent Application Publication number 2003/0148410 A1 (filed November 21, 2002) is withdrawn in light of the cancellation of the claims.

New Grounds of Objections

Claim Objections

6. Claims 1, 4, 7 and 10 are objected to because of the following informality: because the term, "ADAM 12" should be followed with the term "protein" to make clear this particular molecule is being detected. This concept is plain and clear in claim 11, for example. Correction is required.

New and Maintained Grounds of Rejection

Claim Rejections – 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 3, 10-16 and 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1 and 10 recite “detecting the presence or *absence* of ADAM 12”. It is not clear how absence of a non-present molecule is detected. Applicants are requested to clarify.

Claim Rejections – 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The rejection of claims 1, 3, 4, 6, 7, 9-16 and 20-37 under 35 U.S.C. 103(a) as being unpatentable over Iba et al. (Am J. Pathol. 154(5):1489-501, May 1999), and further in view of Berger et al./ U.S. Patent Application Publication number 2003/0148410 A1 (filed November 21, 2002) is maintained. Claims 38-49, 51-53 and 55 have been cancelled.

Applicants disagree with the Examiner’s statement “Applicants have not presented any scientific evidence that teaches away from one of ordinary skill in the art implementing tissue samples to assess ADAM12 expression and diagnosing epithelial cancers” set forth in the Final Action mailed August 23, 2010, page 5, section 6. Applicants note the criteria for the Office making a proper rejection under 35 U.S.C. 103, see bridging paragraph of pages 7 and 8, Remarks submitted February 23, 2011. Applicants further assert Iba mentions

"the membrane-anchored form of (ADAM 12-S) is present in both normal and tumor tissues" and "...the membrane-bound form of ADAM 12 is not expected to be present in biological fluids, one of ordinary skill in the art would not have any expectation of success in diagnosing cancers of epithelial origin by detecting ADAM 12 in biological fluids", see page 8, 1st full paragraph.

Applicants also argue "Berger... focused on the use of colon cells and colon-associated fluids for detecting colon cancer", see Remarks, page 9. These arguments and points of view have been carefully considered, but found unpersuasive.

Applicants are reminded the claims broadly read on a number of fluid biological samples, as well as the broadly termed ADAM 12. The claims do not include a detection step with any particular antibody, which could possibly discriminate between membrane-anchored long form (ADAM 12-L) and the shorter secreted form (ADAM 12-S), nor read on just urine. Notwithstanding, it is art known that cancer cells abrogate organs, vasculature and would be present in fluids, such as sera and blood. Consequently, both forms of ADAM 12 would have a high propensity to be detected and it would be expected by one of ordinary skill in the art to detect the membrane-bound form of ADAM in biological fluids. While Berger does discuss detecting colon cancer, the patent is not devoid of teaching identifying breast cancer with the assaying a urine sample, see page 4, column 0058. For these reasons and the reasons of record the rejection is maintained and reiterated.

Iba teaches “[t]he distribution of ADAM 12 in... 37 human carcinomas compared with the normal counterpart tissue... investigated by immunohistochemistry”, see page 1493, Results section. These tissue specimens are from human carcinomas comprising ductal breast carcinoma, adenocarcinoma of the colon and rectum, squamous cell carcinoma of the lung and adenocarcinoma of the stomach, see page 1490, Tissue samples...section. Adjacent nontumorous tissues were also investigated. “All 15 cases of breast carcinomas exhibited intense ADAM 12 immunoreactivity (Figure 1A) using several different antibodies, whereas in normal breast tissue, only a few scattered luminal cells of the ducts exhibited ADAM 12 immunoreactivity (Figure 1E)”, see page 1493, Results section. Labeled monoclonal antibodies to human ADAM 12 were implemented in the immunohistochemistry assays, see page 1490, Antibodies and Immunohistochemistry...sections; and Figure 1 on page 1494.

Normal and cancerous human breast tissue specimens were analyzed by RT-PCR using specific primers for ADAM 12-L and ADAM 12-S, see last sentence of column 1, page 1493; and Figure 1 on page 1494. “Breast carcinoma tissue appeared to contain more ADAM 12-L transcript than normal breast tissue (Figure 1G)”, see bridging sentence of columns 1 and 2 on page 1493. Iba does not teach fluid biological samples. Iba does not teach the disclosed method, wherein a urine sample is assayed for ADAM 12.

However, Berger teaches urine as a biological sample to test for the presence of ADAM 12. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of both documents assay a plethora of biological samples for ADAM 12, particularly a urine sample. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings because the Berger implemented the diagnostic assay using urine as a test sample and ADAM 12 is clearly and definitively associated with tumor cancer, see publication, page 1, section 0008 and page 33, section 0300; and Iba, abstract.

11. The rejection of claims 1, 3, 4, 6, 7, 9-16 and 20-37 under 35 U.S.C. 103(a) as being unpatentable over Iba et al. (Am J. Pathol. 154(5):1489-501, May 1999), and further in view of WO document, WO 01/66557 A1 (published 13 September 2001/ IDS reference number 3 submitted May 25, 2010) and Berger et al./ U.S. Patent Application Publication number 2003/0148410 A1 (filed November 21, 2002). Claims 38-50 have been cancelled.

Applicants' arguments are similar to those presented in the initial 103(a) rejection. Applicants conclude arguments citing "...the prior art combination would not have yielded predictable results..." and "do not render the instant

claims obvious", see Remarks, page 10. These arguments and points of view have been carefully considered, but found unpersuasive.

Applicants are reminded the claims broadly read on a number of fluid biological samples, as well as the broadly termed ADAM 12. The claims do not include a detection step with any particular antibody, which could possibly discriminate between membrane-anchored long form (ADAM 12-L) and the shorter secreted form (ADAM 12-S), nor read on just urine. Notwithstanding, it is art known that cancer cells abrogate organs, vasculature and would be present in fluids, such as sera and blood. Consequently, both forms of ADAM 12 would have a high propensity to be detected and it would be expected by one of ordinary skill in the art to detect the membrane-bound form of ADAM in biological fluids. While Berger does discuss detecting colon cancer, the patent is not devoid of teaching identifying breast cancer with the assaying a urine sample, see page 4, column 0058. For these reasons and the reasons of record the rejection is maintained and reiterated.

Iba teaches "[t]he distribution of ADAM 12 in... 37 human carcinomas compared with the normal counterpart tissue... investigated by immunohistochemistry", see page 1493, Results section. These tissue specimens are from human carcinomas comprising ductal breast carcinoma, adenocarcinoma of the colon and rectum, squamous cell carcinoma of the lung and adenocarcinoma of the stomach, see page 1490, Tissue samples...section. Adjacent nontumorous tissues were also investigated. "All 15 cases of breast

carcinomas exhibited intense ADAM 12 immunoreactivity (Figure 1A) using several different antibodies, whereas in normal breast tissue, only a few scattered luminal cells of the ducts exhibited ADAM 12 immunoreactivity (Figure 1E)", see page 1493, Results section. Labeled monoclonal antibodies to human ADAM 12 were implemented in the immunohistochemistry assays, see page 1490, Antibodies and Immunohistochemistry...sections; and Figure 1 on page 1494. Iba does not teach the disclosed method, wherein a biological sample assayed for ADAM 12 is urine.

The WO document teaches a protein encoded by gene no: 2 is human ADAM12 protein, see page 12, section 41. Antibodies directed to this protein are used for the diagnosis of diseases in a biological sample, see page 13, section 44; page 14, section 46; page 59, section 178; page 89, section 266; and page 90, sections 267-269. Biological samples include body fluids (such as sera, plasma, urine) and tissue biopsies, see page 97, section 297; page 107, section 329; and pages 108-109. The antibodies can be used in methods of diagnosis of cancers such as gastric, ovarian, lung, liver, breast and bladder, see section 427 bridging section 427. Moreover, Berger discloses not only can colon cancer be diagnosed or identified, but ovarian, lung, cervical, breast and prostate cancer may also be identified using the taught methodology, see page 3, section 0048; page 4, section 0058; and page 11, section 0118. The ADAM 12 marker can be detected blood fluids, stool, colon lavage fluids, lymph fluids

and urine via an antibody which is labeled by several means, see page 3, section 0048; page 10, section 0114; and page 33, section 0300.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine all the teachings of all the documents to assay a plethora of biological samples for ADAM 12, particularly a urine sample, blood or serum. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Berger. Berger implemented a diagnostic assay using urine, blood fluids as test samples and ADAM 12 is clearly and definitively associated with cancer, see WO document; Berger, page 3, section 0048 and page 33, section 0300; and Iba, abstract.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or

patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. The provisional rejection of claims 1, 3, 4, 6, 7, 9-16 and 20-37 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21, 23 and 42 of copending Application No. 12/085,134/ U.S. Patent Application No. 20090215102 (filed April 14, 2009) is maintained. Claims 38-45, 48, 49, 52 and 53 have been cancelled.

Applicants simply assert once the claims are found allowable, Applicants will address the rejection, see Remarks submitted July 19, 2010, page 10. This point of view has been carefully considered, but found unpersuasive. The rejection is maintained for the reasons of record and Applicants' limited response. The rejection is reiterated.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims read detecting ADAM 12 in biological samples.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a *flexible schedule*, however she can normally be reached between the hours of 8 am to 8 pm, Monday through Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Misook Yu, Ph.D. can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Alana M. Harris, Ph.D.
11 March 2011
/Alana M Harris, Ph.D./

Primary Examiner, Art Unit 1643